

# TENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>9803 PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/IL 99/ 00448</b>	International filing date (day/month/year) <b>19/08/1999</b>	(Earliest) Priority Date (day/month/year) <b>21/08/1998</b>
Applicant <b>YEDA RESEARCH AND DEVELOPMENT CO. LTD. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

#### 1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure N .

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ Non of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 99/00448

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Remark: Although claim 18 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2. ☒ Claims Nos.: **1-5, 7, 9, 13**  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-5,7,9,13

Present claims 1-3 and 13 relate to a product defined by reference to a desirable property, namely an anti-inflammatory activity. The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

In addition, present claims 4,5,7,9 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds (pep1) to (pep46) and closely related analogues.

Therefore, claims 6,8,10-12 were searched completely; claims 14-18 only as far as concerning the searched subject-matter.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IL 99/00448

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/55 A61K38/20 C07K5/08 C07K5/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	ARIEL, AMIRAM ET AL: "IL-2 induces T cell adherence to extracellular matrix: inhibition of adherence and migration by IL-2 peptides generated by leukocyte elastase" J. IMMUNOL. (1998), 161(5), 2465-2472 , 1 September 1998 (1998-09-01), XP002133613 the whole document ----	1-18
A	WO 95 00538 A (PEPTECH UK LTD ; IVANOV VADIM TIKHONOVICH (RU); MIKHALEVA INESSA IV) 5 January 1995 (1995-01-05) the whole document ----- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

05/04/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cervigni, S

PGI/IL 99/00448

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>SUZUKI, KAZUO ET AL: "Localization of chemotactic activity and 64 kD protein phosphorylation fo human polymorphonuclear leukocytes in N-terminus of the chemotactic protein LUCT/IL-8"</p> <p>BIOCHEM. BIOPHYS. RES. COMMUN. (1989), 163(3), 1298-305 ,1989, XP002133614 abstract</p> <p>-----</p>	
A	<p>DATABASE WPI</p> <p>Section Ch, Week 199136</p> <p>Derwent Publications Ltd., London, GB;</p> <p>Class B04, AN 1991-262316</p> <p>XP002133615</p> <p>&amp; JP 03 170498 A (TEIKOKU HORMONE MFG CO LTD), 24 July 1991 (1991-07-24)</p> <p>abstract</p> <p>-----</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IL 99/00448

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9500538	A	05-01-1995	AU 6977994 A ZA 9404483 A	17-01-1995 22-12-1995
JP 3170498	A	24-07-1991	NONE	

## PCT

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International application No.

PCT/IL 99/ 00448

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"&" document member of the same patent family

Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

05/04/2000

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cervigni, S

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 99/00448

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	<p>DATABASE WPI Section Ch, Week 199136 Derwent Publications Ltd., London, GB; Class B04, AN 1991-262316 XP002133615 &amp; JP 03 170498 A (TEIKOKU HORMONE MFG CO LTD), 24 July 1991 (1991-07-24) abstract</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IL 99/00448

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9500538	A	05-01-1995	AU	6977994 A	17-01-1995
			ZA	9404483 A	22-12-1995
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JP 3170498	A	24-07-1991	NONE		
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## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 12 April 2000 (12.04.00)	
International application No. PCT/IL99/00448	Applicant's or agent's file reference 9803 PCT
International filing date (day/month/year) 19 August 1999 (19.08.99)	Priority date (day/month/year) 21 August 1998 (21.08.98)
Applicant LIDER, Ofer et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
13 March 2000 (13.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia RANAIVOJAONA Telephone No.: (41-22) 338.83.38
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Set Name Query  
side by side

Hit Count Set Name  
result set

*DB=DWPI; PLUR=YES; OP=ADJ*

L10 derived peptide? and L9 2 L10

L9 (interleukin 2 or il 2 or il-2) 1508 L9

*DB=PGPB; PLUR=YES; OP=ADJ*

L8 derived peptide? and L7 2 L8

L7 (interleukin,2 or il 2 or il-2).ab. 46 L7

*DB=USPT; PLUR=YES; OP=ADJ*

L6 derived peptide? and L5 2 L6

L5 (interleukin 2 or il 2 or il-2).ab. 338 L5

*DB=USPT,PGPB; PLUR=YES; OP=ADJ*

L4 derived peptide? and L3 4 L4

L3 (interleukin 2 or il 2 or il-2).ab. 384 L3

*DB=USPT; PLUR=YES; OP=ADJ*

L2 derived peptide? and L1 280 L2

L1 (interleukin 2 or il 2 or il-2) 9347 L1

END OF SEARCH HISTORY

FAQM Checklist

Appl. Ser. No. ....

5 date

09 / 7 63,293

FD

05/17/01  
~~08/17/99~~

EFD 08/19/99. via .P.C.T..I.L.95/.00448

Briefed ✓

10 Form 948 present? NO

Declaration (06-05)

PCT referred to?

priority dates OK? ✓

continuing dates OK?

15 CIP duty? (06-05-09)

Meets conditions for priority (02-09)

20 Sequences in compliance?

Restriction/Election? ✓

Priority Docs present?

25 File wrapper labeled OK and initialed?

Title (06-11) ✓

30 Abstract (06-12 missing)

(06-13 informs)

(06-14,15 content) ✓

Figures (06-22) ✓

35 Brief Description.

Amendments? ✓

40 IDS checked

Seq Srch requested ✓

Copies of refs requested

45 07-29, 06-31?

07-34

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :

C07K 14/55, A61K 38/20, C07K 5/08,  
5/10

A3

(11) International Publication Number:

WO 00/11028

(43) International Publication Date:

2 March 2000 (02.03.00)

(21) International Application Number:

PCT/IL99/00448

(22) International Filing Date:

19 August 1999 (19.08.99)

(30) Priority Data:

9818370.0

21 August 1998 (21.08.98)

GB

126009

31 August 1998 (31.08.98)

IL

129980

16 May 1999 (16.05.99)

IL

(71) Applicant (for all designated States except US): YEDA RE-  
SEARCH AND DEVELOPMENT CO. LTD. [IL/IL]; Weiz-  
mann Institute of Science, P.O. Box 95, 76100 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): LIDER, Ofer [IL/IL];  
Shikun Banim 119, 76965 Kfar Bilu Bet (IL). ARIEL,  
Amiram [IL/IL]; Hagalil Street 11, 76601 Rehovot (IL).  
HERSHKOVIZ, Rami [IL/IL]; 4 Habaal Shem Tov, 46342  
Herzliya (IL). YAVIN, Eran, J. [IL/IL]; Moskovich Street  
41, 76468 Rehovot (IL). FRIDKIN, Matityahu [IL/IL];  
Miller Street 23, 76284 Rehovot (IL).(74) Agent: BEN-AMI, Paulina; Yeda Research and Development  
Co. Ltd., Weizmann Institute of Science, P.O. Box 95,  
76100 Rehovot (IL).(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG,  
BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE,  
ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,  
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,  
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,  
VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW,  
SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG,  
KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW,  
ML, MR, NE, SN, TD, TG).

Published

With international search report.

(88) Date of publication of the international search report:

6 July 2000 (06.07.00)

(54) Title: ANTI-INFLAMMATORY PEPTIDES DERIVED FROM IL-2 AND ANALOGUES THEREOF

(57) Abstract

Synthetic anti-inflammatory peptides derived from the sequence of IL-2 are provided. Parent peptides of the sequences Ile-Val-Leu, Glu-Phe-Leu-Asn-Arg-Trp-Ile-Thr and Arg-Met-Leu-Thr, were obtained by elastase enzymatic digestion of IL-2, synthesized and modified. The peptides are useful in conditions of acute and chronic inflammation such as in autoimmune diseases.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## INTERNATIONAL SEARCH REPORT

In ☐ national Application No

PCT/IL 99/00448

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/55 A61K38/20 C07K5/08 C07K5/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	ARIEL, AMIRAM ET AL: "IL-2 induces T cell adherence to extracellular matrix: inhibition of adherence and migration by IL-2 peptides generated by leukocyte elastase" J. IMMUNOL. (1998), 161(5), 2465-2472 1 September 1998 (1998-09-01), XP002133613 the whole document	1-18
A	WO 95 00538 A (PEPTECH UK LTD ; IVANOV VADIM TIKHONOVICH (RU); MIKHALEVA INESSA IV) 5 January 1995 (1995-01-05) the whole document  -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

05/04/2000

Name and mailing address of the ISA

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Fax (+31-70) 340-3016

Authorized officer

Cervigni, S

In                     ional Application No                     

**C-(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 99/00448

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim 18 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☒ Claims Nos.: 1-5, 7, 9, 13  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-5,7,9,13

Present claims 1-3 and 13 relate to a product defined by reference to a desirable property, namely an anti-inflammatory activity. The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

In addition, present claims 4,5,7,9 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds (pep1) to (pep46) and closely related analogues.

Therefore, claims 6,8,10-12 were searched completely; claims 14-18 only as far as concerning the searched subject-matter.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

II International Application No  
**PCT/IL 99/00448**

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9500538 A	05-01-1995	AU 6977994 A ZA 9404483 A	17-01-1995 22-12-1995
JP 3170498 A	24-07-1991	NONE	